Managing the Metabolism of Transition Cows

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Summary
Transition cows must exquisitely coordinate their metabolism to meet tremendous increases in nutrient demand during early lactation, particularly the demand for glucose production by liver. Excessive mobilization of nonesterified fatty acids (NEFA) from body fat during the transition period presents challenges to liver function, including the capacity of liver to produce glucose. Strategies to either reduce the supply of NEFA to the liver or optimize the metabolism of NEFA by liver include maximizing dry matter intake of well-formulated transition rations, dietary supplementation with choline, or short-term drenching strategies using propylene glycol. Supplementation of other nutrients (methionine analogs and conjugated linoleic acid) has been shown to improve performance during early lactation; however, their mode of action does not appear to be related directly to liver metabolism. Research investigating nutritional grouping strategies for dry cows indicates that the two-group dry cow system is preferred to a one-group dry cow system; however, there may be interactions of grouping system with body condition score on postpartum performance.

Introduction
Transition cow biology and management has become a focal point for research in nutrition and physiology during the past fifteen years (Bell, 1995; Drackley, 1999; Grummer, 1995; Overton et al., 2000). Several driving forces have underpinned the evolution of this research. First, it was recognized that many of the metabolic disorders afflicting cows during the periparturient period are interrelated in their occurrence (Curtis et al., 1985) and approximately 50% of cows have one or more adverse health events during this period (Ferguson, 2001). Furthermore, of cows that leave dairy herds, approximately 25% leave during the first 60 days in milk (with an uncertain additional percentage of animals leaving dairy herds after 60 days in milk) because of downstream effects of periparturient difficulty (Godden et al., 2002).

For cows to successfully transition to lactation, metabolic adaptations that enable increased synthesis of glucose, mobilization of sufficient (but not excessive) body fat reserves to meet the energetic demands of lactation, and calcium mobilization to meet the increased demands for calcium. The adaptations that must occur in the dairy cow to successfully adapt to increased demand for calcium have been reviewed previously at this conference (Goff, 1999; Goff, 2001). Therefore, the purpose of this paper will be to briefly review the key metabolic adaptations related to energy metabolism that must occur for cows to successfully transition to lactation, provide some insight into "managing metabolism" of transition dairy cows, and to provide some "bottom line" recommendations for ration formulation and grouping of transition cows.

Metabolic Adaptations in Transition Cows
The primary series of metabolic adaptations that must occur to underpin a successful transition to lactation relates to increased glucose synthesis by liver and decreased glucose oxidation by peripheral tissues (i.e., muscle) at the onset of lactation. Glucose represents an overriding metabolic demand during the transition period because of the requirements of the mammary gland for lactose synthesis. Data in Figure 1 indicate that the liver of the cow must more than double its glucose production in the immediate periparturient period in order to meet this demand.

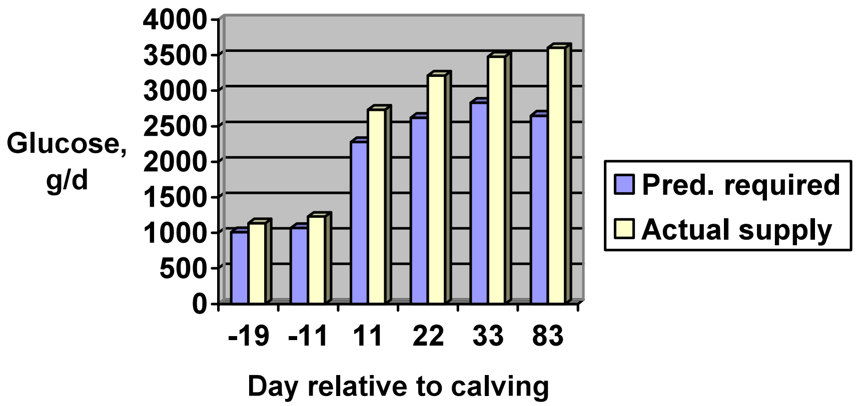


Figure 1. Predicted whole-body glucose requirements compared with actual supply of glucose by gut and liver during the transition period and early lactation. Data are from Reynolds et al. (2000). Predictions are as described by Overton (1998).

A second key metabolic adaptation relates to mobilization of body reserves, particularly body fat stores, in support of the increased energetic demands during early lactation paired with insufficient energy intake. This mobilization of body fat occurs through release of NEFA into the bloodstream (Figure 3). These NEFA are used for energy by body tissues and as precursors for synthesis of milk fat; however, available data suggest that the liver takes up NEFA in proportion to their supply (Emery et al., 1992). Unfortunately, the liver typically does not have sufficient capacity to completely dispose of NEFA through export into the blood or catabolism for energy (Figure 2), and thus transition cows are predisposed to accumulate triglycerides in the liver tissue. The primary consequence of this triglyceride accumulation appears to be impaired liver function, including decreased capacity for ureagenesis and gluconeogenesis.

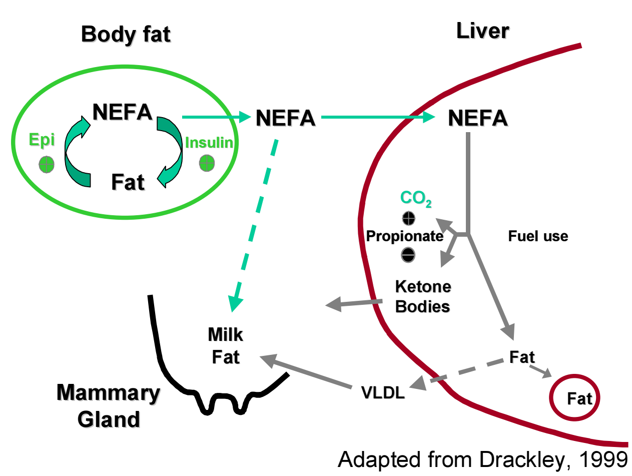


Figure 2. Schematic of metabolism of nonesterified fatty acids (NEFA) in the dairy cow (adapted from Drackley, 1999).

Strategies to Manage Liver Metabolism in Transition Cows

Our guiding principle based collectively upon these data is that management of NEFA during the transition period is an important factor influencing liver health, the capacity of liver to make glucose, and subsequently production and metabolic disorder incidence in transition cows. The two primary approaches that can be taken are:

1) decrease the supply of NEFA to liver through diet and feeding management (perhaps use of glucogenic supplements)
2) optimize capacity of liver to dispose of NEFA either by burning them for fuel or exporting them as triglycerides in lipoproteins (VLDL)

Good close-up and fresh cow nutritional programs, combined with excellent feeding management to achieve high levels of dry matter intake throughout the transition period, achieves 80 to 90% of the potential of the first strategy and should always be the first area of focus for management. Contrary to popular belief, data supporting that niacin supplementation to the diet decreases plasma concentrations of NEFA are limited; nevertheless, a practical recommendation would be to include niacin (12 g/d) in diets fed to herds struggling with overconditioned cows. Glucogenic supplements such as propylene glycol are effective at decreasing concentrations of NEFA and B-hydroxybutyrate (BHBA; the predominant ketone body found in blood); however, propylene glycol must be drenched or fed such that it is consumed as a bolus in order to be effective in decreasing concentrations of NEFA and BHBA (Christensen et al., 1997), and thus presents both cost and labor challenges. The duration of treatment in most experiments reported in the literature ranges from 10 to 40 days per cow. Recently, two experiments have been conducted (Pickett et al., 2002; Stokes and Goff, 2001) that report beneficial effects of drenching propylene glycol beginning on the day of calving and continuing for one or two subsequent days (Figure 3) -- these short-term treatments are much more acceptable from a cost and labor standpoint and have more potential for commercial application.

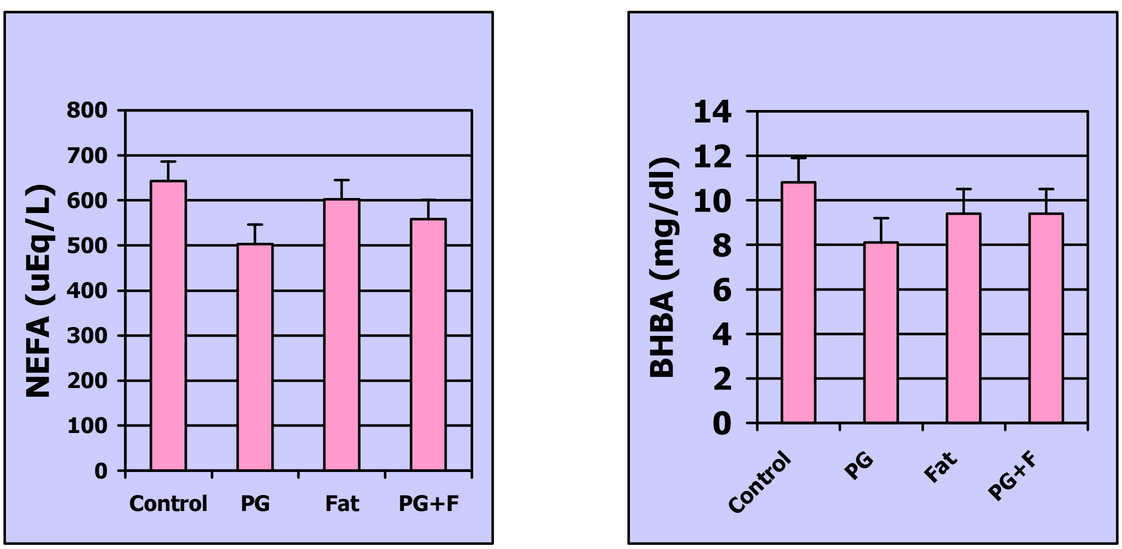


Figure 3. Concentrations of NEFA (left pane) and BHBA (right pane) during the first 21 days postcalving for cows drenched with either a control, propylene glycol (500 ml/day; PG), fat (1 lb/day), or a combination of propylene glycol and fat for the first 3 days postcalving (PG decreased concentrations of NEFA ($P < 0.03$), but did not affect concentrations of BHBA ($P < 0.20$). From Pickett et al. (2002).

Propylene glycol exerts its effects on NEFA primarily by triggering the release of insulin following the bolus of glucose produced when propylene glycol is administered as a drench. Hayirli et al. (2002) recently evaluated administration of slow-release human insulin as a means of decreasing NEFA and triglyceride accumulation. They found that administration of 0.06 IU/lb body weight of slow release insulin on day 3 postcalving decreased plasma NEFA and liver triglyceride concentrations during the first week of lactation, and tended to increase dry matter intake and milk production. Administration of slow release insulin at dosages larger than this dosage decreased dry matter intake and milk production in this study.

In addition to the potential for strategies to increase the concentrations of insulin in transition dairy cows to decrease NEFA, one strategy to increase the effectiveness of insulin has been investigated. Chromium (Cr) has been demonstrated to potentiate insulin action in nonruminants. Two experiments (Hayirli et al., 2001; Smith et al., 2002) demonstrated that administration of up to 0.06 mg of Cr as Cr-methionine per kilogram of metabolic body weight decreased concentrations of NEFA during the prepartum period and resulted in increased dry matter intake and milk production postcalving.

Recently, another strategy related to decreasing energy demands on the transition cow has been suggested to potentially decrease reliance on body reserves and thereby reduce the supply of NEFA to the liver. In typical midlactation cows, approximately 50% of the fatty acids secreted as milk fat are taken up by the mammary gland from the bloodstream as preformed fatty acids. The remaining 50% of fatty acids in milk are synthesized de novo in the mammary gland, and account for approximately 50% of the energetic cost of milk synthesis (NRC, 2001). Conjugated linoleic acids (CLA), specifically the *trans*-10, *cis*-12 isomer of CLA, have been discovered to be potent inhibitors of milk fat synthesis (Bauman et al., 2000). Giesy et al. (1999) fed cows 50 g/d of a mixture of CLA isomers (35% *trans*-10, *cis*-12 by weight) in a Ca-salt form from day 13 through 80 postpartum. They reported few effects of CLA supplementation on cow performance during days 14 through 28 postcalving; however, milk yield was increased, and percentage and yield of milk fat were decreased, during days 35 through 80 postpartum. Energy balance was not affected by treatment during either period. Given that supplementation with CLA in their experiment began after concentrations of NEFA have returned to relatively low levels in the blood (Overton and Piepenbrink, 1999), we hypothesized that supplementation of CLA during the entire transition period and early lactation would be more effective in terms of potentially decreasing energy demand during early lactation. Bernal-Santos et al. (2001) fed cows 30.4 g/day of a mixture of CLA isomers (29% *trans*-10, *cis*-12 by weight) in a Ca-salt form from 14 days before expected calving through 140 days of lactation. Results were similar to those of Giesy et al. (1999) in that milk yield and milk fat percentage during the first two weeks postpartum were not affected by CLA supplementation; however, milk fat percentage was decreased by 13% and milk yield tended to be increased (6.6 lb/day) during the entire postpartum period in cows administered the CLA supplement. Energy balance and concentrations of NEFA and BHBA in plasma were not affected by treatment. Therefore, contrary to our hypothesis, CLA supplementation does not appear to substantially reduce reliance on body fat stores; however, energy spared from milk fat synthesis apparently was redirected to lactose synthesis and may offer the opportunity to use CLA as a management tool to increase peak milk yield.

Even when the first strategy is in place on individual dairy farms, we believe that there are opportunities to further improve liver health by employing nutritional strategies to optimize the capacity of liver to dispose of NEFA rather than accumulate them as fat in liver tissue. As mentioned above, the two disposal routes of NEFA from liver involve burning them for fuel and exporting them back into the blood as triglycerides in very low density lipoproteins (VLDL; Figure 2). Choline, methionine, lysine, and essential fatty acids (linoleic and linolenic acids) all are candidates for modulating these aspects of liver fatty acid metabolism. We determined that choline supplementation to diets fed to transition cows decreased the rate of triglyceride accumulation in liver tissue and tended to quadratically increase milk yield during early lactation (Piepenbrink and Overton, 2002). Methionine supplied as 2-hydroxy-(4-methylthio)-butanoic acid (HMB) did not affect liver fatty acid metabolism; however, milk yield increased in a quadratic fashion to HMB supplementation (Table 1). Mashek et al. (2002) reported recently that addition in vitro of linoleic or linolenic acids altered hepatic fatty acid metabolism; however, the effects of feeding essential fatty acids on liver metabolism in the intact cow are not known. Further research must be conducted to determine the specific roles of choline, methionine, lysine, and essential fatty acids in liver fatty acid metabolism and to determine the interactions among supply of these nutrients.

Table 1. Yields of milk and milk components by cows fed increasing amounts of 2-hydroxy-4-(methylthio)-butanoic acid (HMB) during the transition period and early lactation (Piepenbrink et al., 2001).

	Treatment				Effect, P <		
Item	Control	+ HMB	++ HMB	SEM	TRT Linear	TRT Quad.	TRT x week
Milk, lb/d	92.6	99.2	92.6	2.9	0.99	0.05	0.13
Fat, %	4.20	4.00	4.07	0.13	0.46	0.36	0.80
Fat, lb/d	3.79	3.88	3.70	0.11	0.59	0.32	0.40
3.5% FCM, lb/d	101.4	105.8	100.1	2.6	0.70	0.11	0.28
CP, %	2.80	2.77	2.84	0.06	0.65	0.33	0.26
CP, lb/d	2.56	2.69	2.58	0.09	0.77	0.22	0.69
Lactose, %	4.70	4.69	4.73	0.05	0.62	0.69	0.76
Lactose, lb/d	4.34	4.65	4.39	0.13	0.86	0.05	0.19
Total solids, %	12.46	12.22	12.38	0.19	0.78	0.36	0.94
Total solids, lb/d	11.40	11.99	11.35	0.31	0.94	0.09	0.53

Grouping Strategies and Diet Formulation For Close-Up Cows

Modern dry cow nutritional grouping strategies involve a two-group system -- a "far off" group consisting of cows from dry off through approximately 21 days prepartum and a "close-up" group consisting of cows from approximately 21 days prepartum through parturition. We would recommend energy densities of approximately 0.59 to 0.63 Mcal/lb of net energy for lactation (NE_L) for diets fed to cows in the far off group. Recently, observational studies at Penn State University and the University of Missouri have suggested that feeding close-up diets containing large amounts of nonforage fiber sources may increase dry matter intake of close-up cows compared to close-up diets containing larger amounts of starch-based cereals. We have determined that periparturient dry matter intake and postpartum milk production and composition are comparable when diets based upon nonforage fiber sources or starch-based cereals are fed (Smith et al., 2002); however, we are continuing to investigate the metabolic implications of changing dietary carbohydrate source on postabsorptive metabolism in transition cows. More detailed recommendations for diets fed to close-up cows, with differentiation of mineral composition based upon anionic versus nonanionic approaches to manage hypocalcemia, are provided in Table 2.

More uncertain is the length of time that cows should be fed the close-up diet. Two experiments have been published recently that provide us with some insight on this topic. Robinson et al. (2001) fed cows and first-calf heifers either a control close-up diet or a close-up diet supplemented with additional energy and protein on commercial dairy farms in the western US and determined that there was a significant increase in milk yield over a full lactation when heifers and cows were fed these diets for 15 days compared with 5 days (Figure 4). Additional supplementation of energy and protein to the diet yielded more milk during the full lactation only when it was fed for 15 days prepartum. In a larger study involving over 13,000 cows on five dairy farms in the western US, Corbett (2002) determined that cows increased predicted 305-day milk production (Figure 5) and decreased occurrence of metabolic disorders as they spent up to 21 days in the close-up group (Figure 6).

These experiments, however, did not explore feeding the close-up diet for longer than the 21 day period currently recommended. Mashek and Beede (2001) fed cows on two commercial dairy farms the close-up diet for an average of either 18 days or 37 days prepartum. There was a slight improvement in energy status of cows fed the close-up diet for 37 days prepartum; however, differences in milk production during early lactation were not significant. Health effects were farm-specific -- one farm had an increased incidence of retained placenta when fed the close-up diet for an average of 37 days prepartum.

Table 2. General goals for diet formulation for closeup cows

	Standard	Anionic
• $NE_{L,}$ Mcal/lb	0.72 to 0.74	
• Metabolizable protein, g/d	1100 to 1200	
• NFC, %	34 to 36	
• Dietary Ca, g/d	100	140
• Dietary Ca, %	0.90	1.2
• Dietary P, %	0.3 to 0.4	0.3 to 0.4
• Mg, %	0.4 to 0.42	0.4 to 0.42
• Cl, %	0.3	0.8 to 1.2
• K, %	< 1.3	< 1.3
• Na, %	0.1 to 0.2	
• S, %	0.20	0.3 to 0.4
• Vitamin A (IU/d)	100000	100000
• Vitamin D (IU/d)	30000	30000
• Vitamin E (IU/d)	1800	1800

We recently completed an experiment on two commercial dairy farms in New York involving nearly 350 cows in which we fed cows either a two-group dry cow program or the close-up diet for the entire dry period (Contreras et al., 2002). Differences in productive performance during the first five monthly test days were not significant among treatments. In looking at interactions of body condition score at dry off with performance during the subsequent lactation, we found that cows with initial body condition score less than 3.0 (mean = 2.8) tended to produce more milk (94.8 lb/day versus 91.0 lb/day) across the first five monthly test days than did cows with body condition score of 3.25 or greater (mean = 3.4). Furthermore, a trend existed for an interaction of body condition score at dry off such that thinner cows fed a two-group dry cow program produced the most milk (97.2 lb/day) during the first five monthly test days, cows fed the close-up diet for the entire dry period were intermediate (92.6 lb/day for both body condition score groups), and heavier cows fed a two-group dry cow program produced the least milk (89.5 lb/day) during the first five monthly test days. Thinner cows lost less body condition during early lactation and had reproductive performance comparable to that of heavier cows. The implications of these data are that replenishment of body condition during late lactation to a body condition score of 3.25 or 3.50 as commonly recommended may not be important for productive and reproductive performance if cows are fed "modern" transition cow feeding programs. Secondly, these data also imply that perhaps heavier cows will benefit from spending the entire dry period in the close-up group. Certainly, more research investigating the interactions of body condition score and nutritional strategies for transition cows is merited.

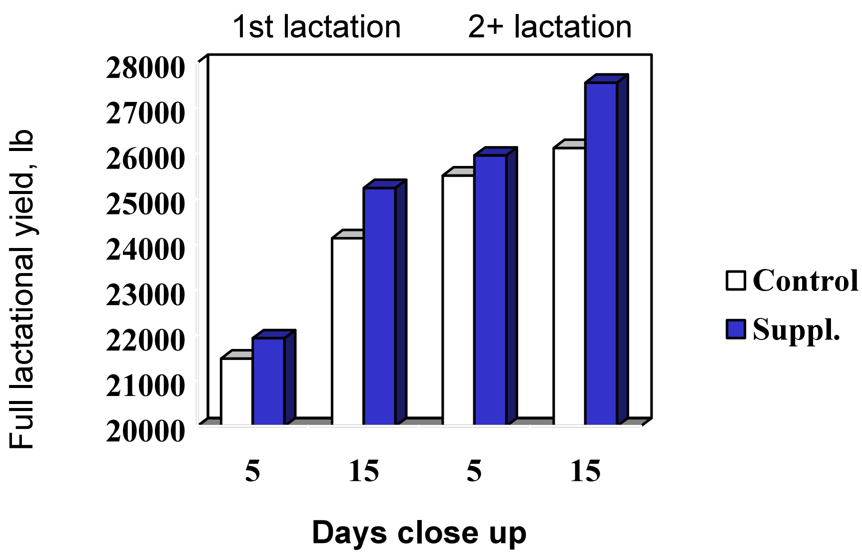
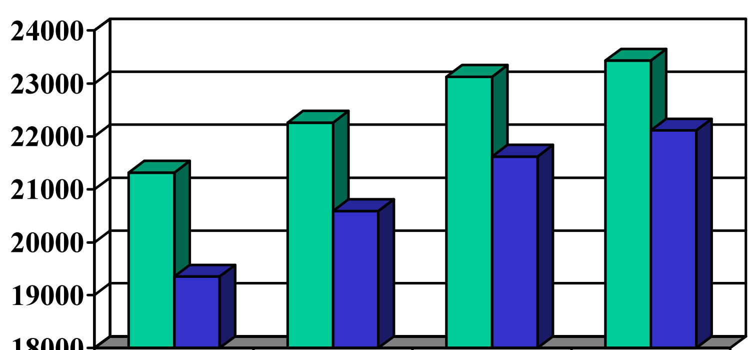
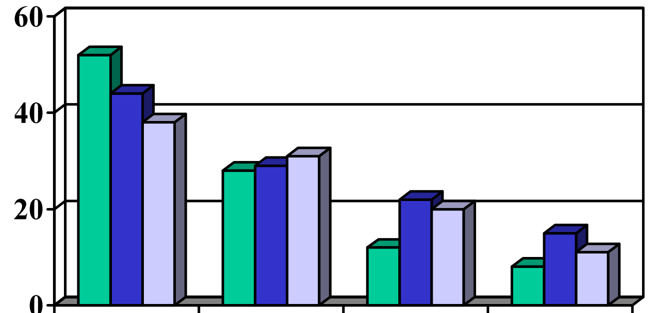


Figure 4. Full lactational milk yields of cows in first and second or greater lactation as affected by feeding either a control or supplemented diet for either 5 or 15 days close-up (Robinson et al., 2001).



	0-7 days	8-14 days	15-21 days	>21 days
Fresh 1-1 to 5-1	21316	22262	23126	23430
Fresh 6-1 to 8-1	19349	20593	21619	22112

Figure 5. Predicted 305-day milk production as affected by days in the close-up group (Corbett, 2002).



	0-7 days	8-14 days	15-21 days	>21 days
Milk Fevers	52	28	12	8
Retained Placentas	44	29	22	15
Uterine Infections	38	31	20	11

Figure 6. Occurrence of metabolic disorders as affected by days in the close-up group (Corbett, 2002).

Current Research and Implications for the Dairy Industry

Currently, our laboratory is engaged in experiments to elucidate the specific roles of individual nutrients in liver metabolism of transition cows and to determine the interactions of metabolism and health that likely provide the biological basis for the myriad of factors that we include in the category of "management" on commercial dairy farms. Collectively, this research will provide much of the basis for managing metabolism of transition dairy cows within transition cow nutrition and management programs in the future.

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